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NEWS 23 JAN 22 CA/CAplus updated with revised CAS roles

NEWS 24 JAN 22 CA/CAplus enhanced with patent applications

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=> s (gtpase and (fluorophor? or fluoresc?))/bi,ab 13325 GTPASE/BI 10106 GTPASE/AB 11161 FLUOROPHOR?/BI 10056 FLUOROPHOR?/AB 465491 FLUORESC?/BI 399940 FLUORESC?/AB L1 646 (GTPASE AND (FLUOROPHOR? OR FLUORESC?))/BI,AB

=> s (exchange (5a) factor?)/bi,ab 570686 EXCHANGE/BI 449760 EXCHANGE/AB 1645878 FACTOR?/BI 1358603 FACTOR?/AB

L2 7675 (EXCHANGE (5A) FACTOR?)/BI,AB

=> s (effector(5a)protein?)/bi,ab 37114 EFFECTOR/BI 33842 EFFECTOR/AB 2325366 PROTEIN?/BI 1848426 PROTEIN?/AB

L3 4136 (EFFECTOR(5A)PROTEIN?)/BI,AB

=> I2 and I3 L2 IS NOT A RECOGNIZED COMMAND The previous command name entered was not recognized by the system

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=> s I2 and I3 L4 159 L2 AND L3

=> 11 and 14

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=> s l1 and l4 L5 5 L1 AND L4

=> d his

(FILE 'HOME' ENTERED AT 20:44:16 ON 22 JAN 2007) FILE 'CAPLUS' ENTERED AT 20:44:31 ON 22 JAN 2007

L1 646 S (GTPASE AND (FLUOROPHOR? OR FLUORESC?))/BI,AB

L2 7675 S (EXCHANGE (5A) FACTOR?)/BI,AB L3 4136 S (EFFECTOR(5A) PROTEIN?)/BI,AB

L4 159 S L2 AND L3 L5 5 S L1 AND L4

=> d l5 1-5 bib ab

L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN AN 2005:1292746 CAPLUS < LOGINID::20070122>> DN 144:32178

TI Methods for identifying chemical modulators of ras superfamily ***gtpase*** activity

IN Sondek, John; Rojas, Rafael

PA The University of North Carolina at Chapel Hill, USA

SO PCT Int. Appl., 47 pp. CODEN: PIXXD2

DT Patent

LA English

FAN. CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ------

Pl WO 2005115482 A2 20051208 WO 2005-US13444 20050419 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, GE, GH, GM, HR, HU, ID, IL, EC, EE, EG, ES, FI, GB, GD, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, MR, NE, SN, TD, TG CF, CG, CI, CM, GA, GN, GQ, GW, ML, PRAI US 2004-564470P P 20040422

AB The invention provides a method of identifying a compd. having the ability to modulate the guanine nucleotide exchange cycle of a Pas superfamily *** GTPase***, comprising: (a) contacting the compd. with a guanine nucleotide

exchange ***factor*** and a ***GTPase*** and obtaining a baseline ***fluorescence*** measurement; (b) contacting the guanine nucleotide ***exchange***

factor and the ***GTPase*** without the commod

factor and the ***GTPase*** without the compd. and obtaining a baseline ***fluorescence*** measurement; (c) adding a ***fluorophore*** -conjugated GTP to the components of (a) and (b), resp.; (d) obtaining
fluorescence measurements of the resp. components of
(c) over time; (e) subtracting the resp. baseline
fluorescence measurements of (a) and (b) from each
fluorescence measurement of (d); and (f) comparing the resulting ***fluorescence*** values of (e), wherein a decrease or increase in the rate of ***fluorescence*** change with the compd. as compared with the rate of
fluorescence change without the compd. identifies a compd. having the ability to modulate the guanine nucleotide exchange cycle of a Ras superfamily ***GTPase***. Further provided are compds. of the invention and pharmaceutical compns. comprising compds. of the invention useful for the treatment of cancer and neurol. disorders.

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN AN 2005;823858 CAPLUS << LOGINI D::20070122>> DN 143:191621

TI Genes differentially expressed in canine osteoarthritis and their use for diagnosis and prognosis

IN Middleton, Rondo P.; Hannah, Steven S.

PA Nestec S.A., Switz.

PRAI US 2004-541346P

SO PCT Int. Appl., 170 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ------

Pl WO 2005075685 A1 20050818 WO 2005-US3375 20050202 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA. GN. GQ. GW. ML. MR. NE. SN. TD. TG AU 2005210503 20050818 AU 2005-210503 20050202 CA 2555083 A1 20050818 CA 2005-2555083 20050202 EP 1711635 A1 20061018 EP 2005-722699 20050202 R: DE, ES, FR, GB, IT, NL

20050202 AB The present invention provides 1558 genes that are differentially expressed in osteoarthritis. RNA was extd. from normal and osteoarthritic canine cartilage chondrocytes, and differential expression detd. by ***fluorescent*** differential display, microarray anal., and quant. PCR. The transcripts may be used for diagnosis and prognosis of osteoarthritis, as well as in methods that may be used to screen test substances for effectiveness in treatment modalities for osteoarthritis. Microarray anal. indicates changes in expression of osteoarthritis-assocd. genes on treatment with chondroitin sulfate, glucosamine, 1,25dihydroxyvitamin D3, 24R,25-dihydroxyvitamin D3, eicosapentaenoic acid, and arachidonic acid. Also described are devices and kits that may be used with the described methods. RE.ONT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE

P 20040202

FORMAT

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

WO 2005-US3375

AN 2004:493871 CAPLUS << LOGINI D::20070122>> DN 141:47303

TI Genetic switches for the detection and elimination of oncogenic fusion proteins, and diagnostic and therapeutic uses thereof

IN Bohlander, Stefan; Froehlich, Nicole

PA Ludwig-Maximilians-Universitaet, Germany

SO PCT Int. Appl., 182 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ------

PI WO 2004050870 20040617 WO 2003-EP13323 20031126 WO 2004050870 A3 20040923 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, ZA, ZM, ZW TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2003289899 A1 20040623 AU 2003-289899 20031126 PRAI EP 2002-27501 20021205 WO 2003-EP13323 20031126

AB The present invention relates to a complex comprising a fusion protein (a) comprising at least two epitopes; (b) protein A comprising an interaction domain capable of interacting with said first epitope of the protein of (a) and comprising a first ***effector*** domain; and (c) ***protein*** B comprising an interaction domain capable of interacting with said second epitope of the protein of (a) and comprising a second effector domain whereby said interaction domains of protein A and protein B are not capable of directly interacting with each other. Furthermore, specific nucleic acid mols, encoding said protein A and/or said protein B are provided as well as expressed protein A/B mols. In addn., compns., in particular pharmaceutical and diagnostic compns, are described which comprise the members of the complex of the present invention. Finally, the invention provides for in vivo and/or in vitro methods for the detection or elimination of a fusion protein, more preferably an oncogenic fusion protein. The detection of the oncogenic fusion proteins BCR-ABL and AML1-ETO was demonstrated in yeast and mammalian cells.

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN AN 2003:207631 CAPLUS << LOGINID::20070122>> DN 138:333795

TI Rational Design of Genetically Encoded *** Fluorescence***
Resonance Energy Transfer-Based Sensors of Cellular Cdc42
Signaling

AŬ Seth, Abhinav; Otomo, Takanori; Yin, Helen L.; Rosen, Michael K.

CS Departments of Biochemistry, Pharmacology, and Physiology, University of Texas Southwestern Medical Center, Dallas, TX, 75390, USA

SO Biochemistry (2003), 42(14), 3997-4008 CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

AB The temporal and spatial control of Rho *** GTPase*** signaling pathways is a central issue in understanding the mol. mechanisms that generate complex cellular movements. The Rho protein Cdc42 induces a significant conformational change in its downstream ***effector***, the Wiskott-Aldrich syndrome *protein*** (WASP). On the basis of this conformational change, we have created a series of single-mol. sensors for both active Cdc42 and Cdc42 guanine nucleotide *** exchange** * * * factors* * * (GEFs) that utilize * * * fluorescence* * * resonance energy transfer (FRET) between cyan and yellow * * * fluorescent * * * proteins. In vitro, the Cdc42 sensors produce up to 3.2-fold FRET emission ratio changes upon binding active Cdc42. The GEF sensors yield up to 1.7-fold changes in FRET upon exchange of GDP for GTP. The GEF-catalyzed rate of nucleotide exchange for the GEF sensor is indistinguishable from that of wild-type Cdc42, but GAP-catalyzed nucleotide hydrolysis is slowed approx. 16-fold. In vivo, both sensors faithfully report on Cdc42 and/or Cdc42-GEF activity. These results establish the successful creation of rationally designed and genetically encoded tools that can be used to image the activity of biol. and medically important mols. in living systems.

RE ONT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE REFORMAT

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN AN 2001:100080 CAPLUS << LOGINID::20070122>> DN 134:264878

TI Rac and phosphatidylinositol 3-kinase regulate the protein kinase B in Fc.epsilon.Rl signaling in RBL 2H3 mast cells AU Djouder, Nabil; Schmidt, Gudula; Frings, Monika; Cavalie, Adolfo; Thelen, Marcus; Aktories, Klaus

CS Institut fur Pharmakologie und Toxikologie der Universitat Freiburg, Freiburg, D-79104, Germany

SO Journal of Immunology (2001), 166(3), 1627-1634 CODEN: JOIMA3; ISSN: 0022-1767

PB American Association of Immunologists

DT Journal

LA English

AB Fc.epsilon.Rl signaling in rat basophilic leukemia cells depends on phosphatidylinositol 3-kinase (PI3-kinase) and the small ***GTPase*** Rac. Here, the authors studied the functional relation among PI3-kinase, its ***effector** *protein*** kinase B (PKB), and Rac using inhibitors of PI3kinase and toxins inhibiting Rac. Wortmannin, an inhibitor of PI3-kinase, blocked Fc.epsilon.RI-mediated tyrosine phosphorylation of phospholipase C.gamma., inositol phosphate formation, calcium mobilization, and secretion of hexosaminidase. Similarly, Clostridium difficile toxin B, which inactivates all Rho GTPases including Rho, Rac and Cdc42, and Clostridium sordellii lethal toxin, which inhibits Rac (possibly Cdc42) but not Rho, blocked these responses. Stimulation of the Fc.epsilon.Rl receptor induced a rapid increase in the GTP-bound form of Rac. Whereas toxin B inhibited the Rac activation, PI3-kinase inhibitors (wortmannin and LY294002) had no effect on activation of Rac. In line with this, wortmannin had no effect on tyrosine phosphorylation of the guanine nucleotide *** exchange*** * factor* * * Vav. Wortmannin, toxin B, and lethal toxin inhibited phosphorylation of PKB on Ser473. Similarly, translocation of the pleckstrin homol, domain of PKB tagged with the green *** fluorescent*** protein to the membrane, which was induced by activation of the Fc.epsilon.Rl receptor, was blocked by inhibitors of PI3-kinase and Rac inactivation. Our results indicate that in rat basophilic leukemia cells Rac and PI3kinase regulate PKB and suggest that Rac is functionally located

upstream and/or parallel of PI3-kinase/PKB in Fc.epsilon.RI signaling.

RE.ONT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE REFORMAT

=> s stibinophenyl?/bi,ab 2 STIBINOPHENYL?/BI 0 STIBINOPHENYL?/AB

L6 2 STI BI NOPHENYL?/BI,AB

=> d l6 1-2 bib ab

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN AN 1987:416741 CAPLUS < LOGINID::20070122>> DN 107:16741

TI Coordination chemistry of higher oxidation states. 25. Synthesis and properties (including cobalt-59 NMR spectra) of cobalt(III) complexes of ligands containing two tertiary stibine groups. Crystal structure of trans-[Co{o-

O6H4(SbMe2)2}2Cl2]2[CoCl4]

AU Jewiss, Hilary C.; Levason, William; Spicer, Mark D.; Webster, Michael

 ${\rm CS}$ Dep. Chem., Univ. Southampton, Southampton, SO9 5NH, LIK

SO Inorganic Chemistry (1987), 26(13), 2102-6 CODEN: INOCAJ; ISSN: 0020-1669

DT Journal

LA English

AB $[Co{o-C6H4(SbMe2)2}2X2]X(X = Cl, Br, I)$ and $[Co\{Me2Sb(CH2)3SbMe2\}2X2]X(X = Br, I)$, were prepd. and shown to have trans pseudooctahedral cations. The prepn. of $trans-[Co{o-C6H4(SbMe2)(PMe2)}2X2]Z(X = CI, Br, I; Z = X,$ BF4), trans-[Co{o-O6H4(PPh2)(SMe)}2X2]BF4, trans-[Co{o-C6H4(PPh2)(SeMe) 2X2] BF4 (X = Cl, Br), and fac-[Co{o-C6H4(PPh2)(SMe)}3](BF4)3 are described. The complexes were characterized by UV-visible spectroscopy and multinuclear (1H, 31P{1H}, 77Se{1H}) NMR as appropriate. 59Co NMR spectra are reported for these complexes, and the characteristic ranges of the 59Co chem. shifts for Co(III) complexes contg. neutral heavy groups VA and VIA donor ligands are established. Crystals of [Co{o-C6H4(SbMe2)2}2Cl2]2[CoCl4] belong to the tetragonal system, space group 141/a, with a 25.264(6), c 9.720(9) .ANG., and Z = 4, R = 0.058 from 1237 obsd. reflections (F > 3.sigma.(F)). The Co of the cation is located on a center of symmetry (Co-Sb = 2.505(1), 2.478(1) .ANG.; Co-Cl = 2.263(4).ANG.), and the anion has .hivin.4 symmetry (Co-Cl = 2.287(6)

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN AN 1960:56170 CAPLUS << LOGINID::20070122>>

DN 54:56170

OREF 54:10915e-h

TI The preparation of p-carboxymethylthiobenzenestibinous compounds

AU Sun, Ts'un-Chi; Chi, Ju-Yun

CS Acad. Sinica, Shanghai

SO Yaoxue Xuebao (1959), 7, 266-9 CODEN: YHHPAL; ISSN: 0513-4870

DT Journal

LA Unavailable

AB p-H2N06H4SCH2CO2H (9.2 g.) was diazotized with 3.5 g. NaNO2 in dil. HCl at -3.degree., added to 12 g. SbCl3 in 40 ml. HCl, and 28 g. glycerol and 96 ml. 35% NaOH added to give 41% crude p-HO2CCH2SO6H4SbO(OH)2 (I), isolated as pyridine salt-HCl, m. 159-60.degree., and purified by dissolving in aq. Na2CO3

and acidifying to give pure I. I decompd. to yield PhSCH2CO2H on redn. with concd. HO and SnO2. However, if redn. of 3 g. I was carried out in 12.5 ml. concd. HO and 25 ml. AcOH at -3.degree. with 2.4 g. SnCl2 in 7.5 ml. of the same acid soln. with const. stirring 1 hr., 47% p-HO2CCH2SO6H4SbCl2 (II), m. 120-2.degree., was obtained. Addn. of 2 g. Kl to 0.3 g. II in dil. HCl gave 85% p-HO2CCH2SC6H4Sbl 2.H2O, m. 106-7.degree., and addn. of 6 ml. 1.4% NH4OH to 0.4 g. II in alc. gave 84% p-HO2CCH2SC6H4SbO.H2O, m. 167-8.degree.. Similarly, 4.1 g. II in 50 ml. H2O added to HSCH2CO2Na (from 2.8 g. acid) with stirring at pH 7 1 hr. and acidified gave 82% p-HO2CCH2SC6H4-Sb(SCH2CO2H)2, m. 187-90.degree., which was dissolved in 1:1 Me2CO-H2O to vield p-HO2CCH2SC6H4Sb.S.CH2.CO.O.H2O, m. 103-5.degree.. Condensation of 1.6 g. II in 25 ml. H2O with HSCH2CH(SH)CO2Na (from 0.61 g. acid) at pH 7 by addn. of NaHCO3 yielded 76% p-HO2CCH2SC6H4I Sb.S.CH2.CH(CO2H).S on acidifying the mixt., m. 145-6.degree.. All these compds. had no chemotherapeutic activity against Schistosomiasis japonica.

=> s (dihydroxy(w)oxido(w)stibino?/bi,ab) 86681 DI HYDROXY 3257 OXI DO 133 STI BI NO?/BI 26 STI BI NO?/AB

L7 0 (DIHYDROXY(W)OXIDO(W)STIBINO?/BI,AB)

=> s (?dihydroxy(w)oxido(w)stibino?)/bi,ab 87383
?DI HYDROXY/BI 42135 ?DI HYDROXY/AB
3257 OXI DO/BI 2609 OXI DO/AB 133
STI BI NO?/BI 26 STI BI NO?/AB
L8 0 (?DI HYDROXY(W)OXI DO(W)STI BI NO?)/BI,AB

=> s (dihydroxy(oxido)stibino)/bi,ab MISSING OPERATOR 'DIHYDROXY(OXIDO' The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s (nsc(w)13778)/bi,ab 3802 NSC/Bl 2554 NSC/AB 7 13778/Bl 3 13778/AB L9 5 (NSC(W)13778)/Bl,AB

=> s nsc13778/bi,ab 2 NSC13778/Bl

NSC13778/AB

L10 2 NSC13778/BI,AB

=> s l9 or l10

L11 6 L9 OR L10

=> d his

(FILE 'HOME' ENTERED AT 20:44:16 ON 22 JAN 2007) FILE 'CAPLUS' ENTERED AT 20:44:31 ON 22 JAN 2007 L1 646 S (GTPASE AND (FLUOROPHOR? OR

FLUORESC?))/BI,AB

L2 7675 S (EXCHANGE (5A) FACTOR?)/BI,AB L3 4136 S (EFFECTOR(5A) PROTEIN?)/BI,AB

L4 159 S L2 AND L3

L5 5 S L1 AND L4

L6 2 S STI BINOPHENYL?/ BI,AB

L7 0 S (DI HYDROXY(W)OXI DO(W)STI BINO?/BI,AB) L8 0 S (?DI HYDROXY(W)OXI DO(W)STI BINO?)/BI,AB

L9 5 S (NSC(W)13778)/BI,AB L10 2 S NSC13778/BI,AB L11 6 S L9 OR L10

=> s I5 and I11

L12 0 L5 AND L11

1

=> d l11 1-6 bib ab

L11 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:120200 CAPLUS << LOGINID::20070122>>

DN 144:205811

TI Assays for identification of topoisomerase inhibitors

IN Stivers, James T.; Kwon, Keehwan

PA The Johns Hopkins University, USA

SO PCT Int. Appl., 81 pp. CODEN: PIXXD2

DT Patent

LA English

Pl WO 2006015369 A2 20060209 WO 2005-US27605 20050803 WO 2006015369 A9 20060330 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, ON, OO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, KG, KZ, MD, RU, TJ, TM PRAI US 2004-598395P P 20040803 US 2004-598398P 20040808 US 2005-693252P 20050623

OS MARPAT 144:205811

AB The instant invention is based, at least in part, on the discovery of a continuous spectroscopic assay for DNA topoisomerase activity. The inventors, for the first time, have demonstrated a multiple turnover assay for DNA topoisomerase using a DNA substrate having one or more ribonucleotide substitutions. Accordingly, in one aspect, the instant invention

substitutions. Accordingly, in one aspect, the instant invention provides a method for measuring the activity of a topoisomerase by contacting a topoisomerase with a duplex nucleic acid mol. that allows for multiple turnover of the topoisomerase comprising a fluorescent moiety covalently attached to one strand of the duplex nucleic acid mol. and a fluorescence quencher covalently attached to the complimentary strand of the duplex nucleic acid mol., wherein topoisomerase activity results in measurable fluorescence from the fluorescent moiety, and measuring the fluorescence of the fluorescent moiety, thereby measuring the activity of the topoisomerase. These assays allow for high throughput screening methods to identify inhibitors of topoisomerase. Accordingly, the instant invention provides screening methods, methods of treating topoisomerase assocd. diseases and disorders, compns. for the treatment of topoisomerase assocd. diseases and disorders, kits to screen for inhibitors of topoisomerase, pharmaceutical compns. for the treatment of topoisomerase assocd, diseases and disorders, and kits comprising pharmaceutical compns. for the treatment of

L11 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:104370 CAPLUS << LOGINI D::20070122>>

topoisomerase assocd. diseases and disorders.

DN 144:246602

TI Novel and specific inhibitors of a poxvirus type I topoisomerase

AU Bond, Alexis; Reichert, Zachary; Stivers, James T.

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SO Molecular Pharmacology (2006), 69(2), 547-557 CODEN: MOPMA3; ISSN: 0026-895X

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

AB Vaccinia DNA topoisomerase (vTopo) is a prototypic pox virus family topoisomerase that shares extensive structural and mechanistic properties with the human type IB enzyme (hTopo) and is important for viral replication. Despite their far-reaching similarities, vTopo and hTopo have surprisingly distinct pharmacol. properties. To further exploit these differences, the authors have developed recently the first high-throughput screen for vTopo, which has allowed rapid screening of a 1990-member small-mol. library for inhibitors. Using this approach, 21 compds. were identified with I C90 values less than 10 .mu.M, and 19 of these were also found to inhibit DNA supercoil relaxation by vTopo. Four of the most potent compds. were completely characterized and are structurally novel topo I inhibitors with efficacies at nanomolar concns. These inhibitors were highly specific for vTopo, showing no inhibition of the human enzyme even at 500- to 2000-fold greater concns. The authors describe a battery of efficient expts. to characterize the unique mechanisms of these vTopo inhibitors and discuss the surprising promiscuity of this enzyme to inhibition by structurally diverse small mols.

RE.ONT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE REFORMAT

L11 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN AN 2005:421165 CAPLUS << LOGINID::20070122>> DN 143:71062

TI Discovery of small-molecule human immunodeficiency virus type 1 entry inhibitors that target the gp120-binding domain of CD4

AU Yang, Quan-en; Stephen, Andrew G.; Adelsberger, Joseph W.; Roberts, Paula E.; Zhu, Weimin; Currens, Michael J.; Feng, Yaxiong; Crise, Bruce J.; Gorelick, Robert J.; Rein, Alan R.; Fisher, Robert J.; Shoemaker, Robert H.; Sei, Shizuko CS Laboratory of Antiviral Drug Mechanisms, SAIC-Frederick, Frederick, MD. USA

SO Journal of Virology (2005), 79(10), 6122-6133 CODEN: JOVI AM; ISSN: 0022-538X

PB American Society for Microbiology

DT Journal

LA English

AB The interaction between human immunodeficiency virus type 1 (HIV-1) gp120 and the CD4 receptor is highly specific and involves relatively small contact surfaces on both proteins according to crystal structure anal. This molecularly conserved interaction presents an excellent opportunity for antiviral targeting. Here the authors report a group of pentavalent antimony-contg. small mol. compds., * * * NSC* * *** 13778*** (mol. wt., 319) and its analogs, which exert a potent anti-HIV activity. These compds. block the entry of X4-, R5-, and X4/R5-tropic HIV-1 strains into CD4+ cells but show little or no activity in CD4-neg. cells or against vesicular stomatitis virus-G pseudotyped virions. The compds. compete with gp120 for binding to CD4: either immobilized on a solid phase (sol. CD4) or on the T-cell surface (native CD4 receptor) as detd. by a competitive gp120 capture ELISA or flow cytometry. * * * NSC* * * * * * 13778 * * * binds to an N-terminal two-domain CD4 protein, D1/D2 CD4, immobilized on a surface plasmon resonance sensor chip, and dose dependently reduces the emission intensity of intrinsic tryptophan fluorescence of D1/D2

CD4, which contains two of the three tryptophan residues in the gp120-binding domain. Furthermore, T cells incubated with the compds. alone show decreased reactivity to anti-CD4 monoclonal antibodies known to recognize the gp120-binding site. In contrast to gp120-binders that inhibit gp120-CD4 interaction by binding to gp120, these compds. appear to disrupt gp120-CD4 contact by targeting the specific gp120-binding domain of CD4.

NSC

13778

may represent a prototype of a new class of HIV-1 entry inhibitors that can break into the gp120-CD4 interface and mask the gp120-binding site on the CD4 mols., effectively repelling incoming virions.

RE.ONT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE REFORMAT

L11 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN AN 2005:331966 CAPLUS << LOGINI D:: 20070122>> DN 143:55899

TI A high-throughput fluorescence-anisotropy screen that identifies small molecule inhibitors of the DNA binding of B-ZIP transcription factors

AU Rishi, Vikas; Potter, Timothy; Laudeman, Julie; Reinhart, Russel; Silvers, Thomas; Selby, Michael; Stevenson, Timothy; Krosky, Paula; Stephen, Andrew G.; Acharya, Asha; Moll, Jon; Oh, Won Jun; Scudiero, Dominic; Shoemaker, Robert H.; Vinson, Charles

CS Laboratory of Metabolism, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA SO Analytical Biochemistry (2005), 340(2), 259-271 CODEN: ANBCA2: ISSN: 0003-2697

PB Elsevier

DT Journal

LA English

AB We have developed a high-throughput fluorescence anisotropy screen, using a 384-well format, to identify small mols. that disrupt the DNA binding of B-ZIP proteins. Binding of a B-ZIP dimer to fluorescently labeled DNA can be monitored by fluorescence anisotropy. We screened the National Cancer Institute diversity set of 1990 compds. to identify small mols. that disrupt the B-ZIP| DNA complex of CREB, C/EBP.beta., VBP, and AP-1 (FOS JUND) bound to their cognate DNA sequence. We identified 21 compds. that inhibited the DNA binding of at least one B-ZIP protein, and 12 representative compds. were grouped depending on whether they displaced ethidium bromide from DNA. Of the 6 compds, that did not displace ethidium bromide, 2 also inhibited B-ZIP binding to DNA in a secondary electrophoretic mobility shift assay screen with some specificity. Thermal stability monitored by CD spectroscopy demonstrated that both compds. bound the basic region of the B-ZIP motif. *** NSC13778*** preferentially binds C/EBP.alpha. 1000-fold better than it binds C/EBP.beta. Chimeric proteins combining C/EBP.alpha. and C/EBP.beta. mapped the binding of *** NSC13778*** to three amino acids immediately N terminal of the leucine zipper of C/EBP.alpha. These expts. suggest that the DNA binding of B-ZIP transcription factors is a potential target for clin. intervention.

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L11 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN AN 2004:331936 CAPLUS << LOGINI D::20070122>> DN 140:350529

TI Stibonic acid compounds and diphenyl compounds for inhibiting viral replication

IN Shoemaker, Robert H.; Ourrens, Michael; Rein, Alan; Feng, Ya-Xiong; Fisher, Robert; Stephen, Andrew; Worthy, Karen; Sei, Shizuko; Orise, Bruce; Henderson, Louis E.

PA United States Dept. of Health and Human Services, USA

SO PCT Int. Appl., 34 pp. CODEN: PIXXD2

DT Patent

LA English

PI WO 2004032869 A2 20040422 WO 2003-US332086 20031008 WO 2004032869 A3 20060302 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, SY, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, ZA, ZM, ZW UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2003279916 20040504 AU 2003-279916 20031008 EP 1575549 Α1 20050921 EP 2003-773233 20031008 CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK US 2006263772 A1 20061123 US 2005-528747 20050322

PRAI US 2002-416854P P 20021008 WO 2003-US32086 W 20031008

OS MARPAT 140:350529

AB The invention provides methods and pharmaceutical compns. for inhibiting viral replication, particularly retroviral replication, e.g. HIV-1 replication. The methods comprise administration of stibonic acid or di-Ph compds. that disrupt viral nucleocapsid binding to nucleic acids.

L11 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN AN 2003:537457 CAPLUS << LOGINID::20070122>> DN 140:283627

TI Analysis of Stibonic Acids by I on Exchange Chromatography with ESI-MS/Photodiode Array Detection

AU Simmons, T. Luke; McCloud, Thomas G.

CS SAIC-Frederick, Inc., NCI-Frederick Cancer Research and Development Center, Frederick, MD, 21702, USA

SO Journal of Liquid Chromatography & Related Technologies (2003), 26(13), 2041-2051 CODEN: JLCTFC; ISSN: 1082-6076 PB Marcel Dekker, Inc.

DT Journal

LA English

AB A method utilizing the counter anion exchange properties of aq. ammonium acetate at pH 9, increasing in concn. linearly from 0 to 0.1 M NH4OAc, using a Hamilton PRP-X100 anion exchange column is presented for the resoln. of arom. stibonic acids and their detection by UV and ESI mass spectrometry. Addnl. phase-bonded silica or polymer backed C8 and C18 column types, eluted with various counter ion solns. (KQO4, NH4COOH, NaOH, NaH2PO4) were evaluated for suitability for stibonic acid anal. RE.ONT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE REFORMAT

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